

Attorney Docket No.: **RU-0170**
Inventors: **Lam and del Pozo**
Serial No.: **10/009,472**
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REMARKS

Claims 1 and 4-9 are pending in the instant application. Claims 1 and 4-9 have been rejected. No new matter has been added by this amendment. Reconsideration is respectfully requested in light of the following remarks.

I. Rejection of Claims Under 35 U.S.C. §103

The rejection of claims 1, 4-5 and 9 under 35 U.S.C. §103(a) as being unpatentable over Xu et al. ((1998) *Nucleic Acids Res.* 26:2034-2035), Mattioni et al. ((1994) *Meth. Cell Biol.* 43:335-352) and Hull et al. ((1995) *Meth. Mol. Biol.* 49:125-141) has been maintained.

The Examiner maintains that with these references in hand it would have been obvious to one of ordinary skill in the art to combine the teachings and arrive at a fusion protein as recited by claims 1, 4-5 and 9. It is suggested that, based on the method of Xu et al., it would have been obvious to those skilled in the art to replace the reporter and the repressor taught by Xu et al. (i.e., enhanced green fluorescent protein, EGFP, and enhanced blue fluorescent protein, EBFP) with the β -glucuronidase taught by Hull et al. and the enzyme repressors taught by Mattioni et al. to construct a fusion protein comprising β -glucuronidase and a hormone binding domain, such as the GR-HBD, linked through a predetermined protease cleavage site such as that of a specific caspase and use it to determine the presence of said protease. It is further suggested that one would have been motivated to do so in order to develop an alternate system to that developed by Xu et al., i.e., an enzyme-based fusion protein and assay, as opposed to the fluorescent protein-based fusion protein and assay

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as developed by Xu et al. In response to Applicants' arguments filed 4/11/05, the Examiner suggests Applicants' indication that Xu et al. must teach that chimeric fluorescent fusion proteins fused through a linker peptide can be replaced with a chimeric beta-glucuronidase in order for the invention to be obvious is misplaced. It is suggested that there is no requirement for a reference to teach equivalency because of the way the invention is claimed. It is further suggested that Applicants' argument which indicates that Hull et al. do not contribute to the obviousness because the reference does not describe "monitoring real-time changes in activity...in living cells over time" is also highly misplaced. The Examiner suggests that the instant claims are not limited to such characteristics or properties of the fusion protein. Applicants respectfully traverse this rejection.

MPEP 2143.01 states that the prior art must suggest the *desirability* of the claimed invention and that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *in re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

The basis of the Examiner's rejection is that it would have been obvious to replace the reporter and the repressor taught by Xu et al. with the β -glucuronidase reporter taught by Hull et al. and the enzyme repressors taught by Mattioni et al. Therefore, the Examiner is suggesting equivalency in the reporter and

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repressor of Xu et al. and the reporter and repressor of Hull et al. and Mattioni et al. However, Applicants maintain that such equivalency does not exist because by modifying the construct of Xu et al. in accordance with the claimed construct, the modified construct would be unsatisfactory for its intended use set forth by Xu et al. In making a modification to a prior art reference to arrive at the claimed invention, MPEP 2143.01 states that if the "proposed modification would render the prior art invention being modified unsatisfactory for its intended use, then there is no suggestion or motivation to make the proposed modification." In this regard, Xu et al. indicate that the assay taught therein is a convenient assay with the major advantage being the use of fluorescent proteins which require no cell staining and the ability to continuously monitoring live cells during the course of an experiment (see page 2035, column 1, ¶2). By modifying this assay in accordance with the claimed invention, the assay of Xu et al. would be unsatisfactory for its intended use because the beta-glucuronidase of Hull et al. requires cell staining and is not useful for monitoring live cells during the course of an experiment. Accordingly, there is no suggestion or motivation in the cited prior art references to make the proposed modification and therefore these references fail to make obvious the instant invention. It is therefore respectfully requested that this rejection be reconsidered and withdrawn.

Claims 6-8 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Xu et al., Mattioni et al. and Hull et al. as applied to claims 1-2, 4-5 and 9 and further in view of the common knowledge in the art.

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The Examiner suggests that using the teachings of Xu et al., Mattioni et al. and Hull et al. it would have been obvious to those skilled in the art to have multiple reporter domains such that the signal intensity obtained from the reporter domain, whether via fluorescence as in Xu et al. or activity of the reporter enzyme as in the instant case, would be more intense and its detection be easier. The Examiner further suggests that because of the simplicity and ease of use of the technique it would have been obvious to one of skill in the art to use multiple protease cleavage sites and detect the presence of multiple sets of proteases. The Examiner indicates that one of skill in the art would have been motivated to do so in order to develop intense signal during the assay. Applicants respectfully traverse this rejection.

Applicants maintain that claims 6-8 fail to be obvious in light of the teachings of Xu et al., Mattioni et al. and Hull et al. for the reasons set forth above in that these references fail to teach, suggest, or motivate the skilled artisan to combine the teachings of the cited references to arrive at the instant inventive chimeric protein of claim 1. Thus, when an independent claim is nonobvious under 35 U.S.C. §103, then any claim depending therefrom is nonobvious. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988). See MPEP §2143.03. Thus, withdrawal of the rejection of claims 6-8 is respectfully requested.

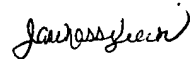
II. Conclusion

The Applicants believe that the foregoing comprises a full and complete response to the Advisory Action of record.

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Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,



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